

CLAIMS

What is claimed is:

1. A method of identifying a ligand having binding specificity a protein isoform in a sample, comprising:

- a. contacting one or more ligands with the sample containing at least two protein isoforms under conditions allowing formation of one or more complexes between the one or more ligands and one or more protein isoforms;
- b. contacting the one or more complexes with a first detectable marker under conditions allowing generation of a first detectable signal and detecting a presence or absence of the first detectable signal;
- c. transferring the one or more protein isoforms from a first support to a second support;
- d. contacting the transferred isoforms with a second detectable marker under conditions allowing generation of a second detectable signal and detecting a presence or absence of the second detectable signal;
- e. comparing the first signal to the second signal, wherein the presence or absence of the first signal and the presence or absence of the second signal identifies the one or more ligands having binding specificity for the one or more protein isoforms.

2. The method of Claim 1, wherein the one or more protein isoform is an isoform of a prion protein.

3. The method of Claim 1, wherein the one or more protein isoform is an isoform of a prion protein selected from the group consisting of PrPc, PrPsc, PrPr, and PrPres.

4. The method of Claim 1, wherein the one or more protein isoform is a PrPsc isoform of a prion protein .

5. The method of Claim 1, wherein the first and the second detectable markers are antibodies.

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6. The method of Claim 1, wherein the first and the second detectable markers detect different isoforms of a same protein.
7. The method of Claim 1, wherein the ligand is immobilized directly on the first support.
8. The method of Claim 1, wherein the ligand is immobilized indirectly on the first support.
9. The method of Claim 1, wherein the ligand is bound to a solid phase that is immobilized on the first support.
10. The method of Claim 1, wherein the one or more ligands are immobilized on the first support prior to contacting the one or more ligands with the sample containing the one or more protein isoforms.
11. The method of Claim 1, wherein the one or more ligands are immobilized on the first support after contacting the one or more ligands with the sample containing the one or more protein isoforms and formation of the one or more complexes.
12. The method of Claim 1, wherein the one or more protein isoforms are modified to form one or more different protein isoforms after the complex is contacted with the first detectable marker, and the one or more different protein isoforms are contacted with the second detectable marker.
13. The method of Claim 12, wherein the one or more protein isoforms are modified by digestion.
14. The method of Claim 12, wherein the one or more protein isoforms are modified by denaturation.
15. The method of Claim 12, wherein the one or more protein isoforms are modified to form the one or more different protein isoforms before, during or after transfer to the second support.

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~~17~~. The method of Claim 1, wherein the ligand identified as having binding specificity for the one or more protein isoform is a peptide having an amino acid sequence selected from the group consisting of SEQ ID NOS:1-22.

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~~18~~. The method of Claim 1, wherein the ligand identified as having binding specificity for the one or more protein isoforms is a peptide having the amino acid sequence SEQ ID NO:3 or its analogs.

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~~19~~. The method of Claim 1, wherein the ligands comprise a plurality of ligands that form an array on the first support.

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